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EXAMINER	
LU, FRANK WEI MIN	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 03/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/978,261	ZHANG, DAVID Y.	
	Examiner	Art Unit	
	Frank W Lu	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 December 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *40-52* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *40-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12/6/2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Applicant's response to the office action filed on December 6, 2004 has been entered. The claims pending in this application are claims 40-52. Rejection and/or objection not reiterated from the previous office action are hereby withdrawn in view of the amendment filed on December 6, 2004.

Drawings

2. Newly submitted Figure 13 has been accepted by the office.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 47, 48, 51, and 52 are rejected under 35 U.S.C. 102(b) as being anticipated by Wang *et al.,* (US Patent NO. 5,567,583, published on October 22, 1996).

Wang *et al.,* teach methods for reducing non-specific priming in DNA detection.

Regarding claim 47, since Wang *et al.,* teach a method for detecting a target nucleic acid, which method comprises the steps of: amplifying the target nucleic acid to obtain an amplification product using a polymerase, a first primer with or without a segment noncontiguous to a first priming sequence, and a second primer with or without a segment

noncontiguous to a second priming sequence in the presence of an oligonucleotide which is incapable of acting as a primer for said polymerase, wherein said oligonucleotide has at least 5 consecutive nucleotides fully complementary to at least 5 consecutive nucleotides of said first primer; and detecting the presence of the target nucleic acid by monitoring the amplification thereof wherein a first fluorophore is covalently attached to said first primer and a second fluorophore is covalently attached to said oligonucleotide, with one of said first and second fluorophores being a donor fluorophore and the other being an acceptor fluorophore, so that when said first primer and said oligonucleotide are hybridized, said donor fluorophore and said acceptor fluorophore are in close proximity to allow resonance energy transfer therebetween; and, further, said detecting step is performed by monitoring fluorescent emission change of said acceptor fluorophore upon irradiation of said donor fluorophore with an excitation light, said change being a function of the extent of said first primer being dissociated from said oligonucleotide and being incorporated into said amplification product of the target nucleic acid (see columns 19 and 20, claims 1 and 3, column 3, second paragraph, and Figure 1), Wang *et al.,* disclose contacting the nucleic acid with an oligonucleotide primer pair comprising a first primer (ie., the first primer taught by Wang *et al.,*) and a second primer (ie., the oligonucleotide taught by Wang *et al.,*) under conditions that allow hybridization between complementary sequences in the target nucleic acid and the oligonucleotide primer pair wherein (i) the first primer of the pair comprises (A) a first sequence that is complementary to the target nucleic acid (ie., the first priming sequence taught by Wang *et al.,*), (B) a second sequence that is complementary to the second primer of the pair (ie., at least 5 consecutive nucleotides of said first primer taught by Wang *et al.,*), and (C) a signal generating moiety (ie., the first fluorophore

taught by Wang *et al.*,); (ii) the second primer of the pair (ie., the oligonucleotide taught by Wang *et al.*,) comprises (A) a sequence that is complementary to the first primer (ie., at least 5 consecutive nucleotides fully complementary to at least 5 consecutive nucleotides of said first primer taught by Wang *et al.*,); and (B) a moiety capable of quenching, masking or inhibiting the activity of the signal generating moiety when located adjacent to, or in close proximity to the signal generating moiety (ie., the second fluorophore taught by Wang *et al.*,); and (iii) when the first primer and the second primer are bound to one another, the signal is inhibited (ie., one of said first and second fluorophores being a donor fluorophore and the other being an acceptor fluorophore and causing fluorescence energy transfer); adding a single stranded oligonucleotide primer comprising sequences complementary to the target nucleic acid (ie., the second primer taught by Wang *et al.*,); adding a DNA polymerase; and amplifying the target nucleic acid and separating the signal generating moiety (ie., the donor fluorophore taught by Wang *et al.*,) and the quenching, masking or inhibitory moiety (ie., an acceptor fluorophore taught by Wang *et al.*,); thereby generating a signal, wherein detection thereof indicates the presence of the target nucleic acid in the sample as recited in claim 47.

Regarding claim 48, Wang *et al.*, teach that the signal generating moiety (ie., the first fluorophore on the first primer taught by taught by Wang *et al.*,) is a fluorescent agent (see columns 19 and 20, claims 1 and 3).

Regarding claims 51 and 52, Wang *et al.*, teach that the target nucleic acid is amplified using polymerase chain reaction (see column 2, lines 32-39).

Therefore, Wang *et al.*, teach all limitations recited in claims 47, 48, 51, and 52.

Response to Arguments

In page 7, last paragraph bridging to page 10, second paragraph of applicant's remarks, applicant argues that: (1) "[A]pplicants maintain that Wang does not teach limitation of step (a) of claim 47 (i.e., contacting the nucleic acid with an oligonucleotide primer pair under conditions that allow hybridization between complementary sequences in the target nucleic acid and the oligonucleotide primer pair). Wang teaches the use of a blocking oligonucleotide which functions to prevent binding of the double-stranded primer to the target nucleic acid (column 5, lines 30 - 36), therefore the primer of the Wang method can only bind to the target nucleic acid as a single-stranded entity (Figure 1). In contrast, claim 47 recites that the target nucleic acid and the primer pair are contacted under conditions that allow hybridization between the target nucleic acid and the primer pair. Accordingly, Wang does not anticipate claim 47 because Wang does not teach each and every element of the claim. Specifically, Wang does not teach the limitation of step (a) of claim 47. Furthermore, Applicants maintain that Wang does not teach limitation (a)(ii)(B) (i.e., a moiety capable of quenching, masking or inhibiting the activity of the signal generating moiety when located adjacent to, or in close proximity to the signal generating moiety) or limitation (a) (iii) (when the first primer and the second primer are bound to one another, the signal is inhibited). The Examiner alleged that the acceptor fluorophore taught by Wang anticipates the "quenching moiety" limitation, however, Wang does not teach that the acceptor fluorophore actually quenches that signal of the donor fluorophore. Indeed, all of the examples in Wang disclose a donor:acceptor pair that displays a signal when in close proximity to each other and that the signal decreases upon amplification of the target nucleic acid (Example IV, column 12, lines 59 - 63; Figure 5). This is indirect contrast to the primer pair of the claimed invention whereby the primer pair displays no signal when the first primer and the second primer

are bound to one another and only exhibits a signal upon amplification of the target nucleic acid (i.e., when the signal generating moiety is separated from the inhibitory moiety). Accordingly, Wang does not anticipate claim 47 because Wang does not teach each and every element of the claim. Specifically, Wang does not teach the limitation of steps (a)(ii)(B) and (a) (iii) of claim 47"; (2) "[W]ang does not teach limitation (d) of claim 47 (i.e., amplifying the target nucleic acid and separating the signal generating moiety and the quenching, masking or inhibitory moiety, thereby generating a signal, wherein detection thereof indicates the presence of the target nucleic acid in the sample)" since "[W]ang discloses a donor:acceptor pair that displays a signal when in close proximity to each other and whose signal decreases upon amplification of the target nucleic acid"; and (3) "[W]hile performing the Wang method, one would have to measure a decrease in signal, which is inherently ambiguous and not as advantageous as measuring an increase in signal. The decrease in signal could mean that one has a positive result or it could indicate that the assay did not adequately perform".

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection. First, since Wang *et al.*, teach amplifying the target nucleic acid to obtain an amplification product using a polymerase, a first primer with or without a segment noncontiguous to a first priming sequence, and a second primer with or without a segment noncontiguous to a second priming sequence in the presence of an oligonucleotide which is incapable of acting as a primer for said polymerase, wherein said oligonucleotide has at least 5 consecutive nucleotides fully complementary to at least 5 consecutive nucleotides of said first primer (see columns 19 and 20, claims 1 and 3, column 3, second paragraph), Wang *et al.*, disclose contacting the nucleic acid with an oligonucleotide primer pair comprising a first primer

(ie., the first primer taught by Wang *et al.,*) and a second primer (ie., the oligonucleotide taught by Wang *et al.,*) under conditions that allow hybridization between complementary sequences in the target nucleic acid and the oligonucleotide primer pair. Second, since Wang *et al.,* teach that said oligonucleotide has at least 5 consecutive nucleotides fully complementary to at least 5 consecutive nucleotides of said first primer, a strand of the target nucleic acid, said first primer and said oligonucleotide forms a triplex wherein said oligonucleotide indirectly binds to the strand of the target nucleic acid by said first primer. Furthermore, claim 47 does not require that the second primer (ie., said oligonucleotide) must directly bind to a strand of the target nucleic acid and the phrase "contacting the nucleic acid with an oligonucleotide primer pair under conditions that allow hybridization between complementary sequences in the target nucleic acid and the oligonucleotide primer pair" in step (a) of claim 47 is a method step for contacting the nucleic acid with an oligonucleotide primer pair and does not mean that both said first primer and said second primer must directly bind to the target nucleic acid. Third, since Wang *et al.,* teach that a first fluorophore is covalently attached to said first primer and a second fluorophore is covalently attached to said oligonucleotide, with one of said first and second fluorophores being a donor fluorophore and the other being an acceptor fluorophore, so that when said first primer and said oligonucleotide are hybridized, said donor fluorophore and said acceptor fluorophore are in close proximity to allow resonance energy transfer therebetween (see columns 19 and 20, claims 1 and 3, column 3, second paragraph), Wang *et al.,* discloses a moiety (ie., said second fluorophore) capable of quenching, masking or inhibiting the activity of the signal generating moiety when located adjacent to, or in close proximity to the signal generating moiety (ie., said first fluorophore) as recited in (a) (ii) of claim 47. Since Wang *et al.,* teach one of said

first and second fluorophores being a donor fluorophore and the other being an acceptor fluorophore, Wang *et al.,* discloses that, when the first primer and the second primer are bound to one another, the signal (ie., the signal generating moiety or said first fluorophore) is inhibited as recited in (a) (iii) of claim 47 wherein the acceptor fluorophore actually quenches that signal of the donor fluorophore. Fourth, claim 47 does not require that the primer pair displays no signal when the first primer and the second primer are bound to one another and only exhibits a signal upon amplification of the target nucleic acid as argued by applicant. Fifth, since Wang *et al.,* teach that said detecting step is performed by monitoring fluorescent emission change of said acceptor fluorophore upon irradiation of said donor fluorophore with an excitation light, said change being a function of the extent of said first primer being dissociated from said oligonucleotide and being incorporated into said amplification product of the target nucleic acid (see columns 19 and 20, claims 1 and 3, column 3, second paragraph), Wang *et al.,* disclose amplifying the target nucleic acid and separating the signal generating moiety and the quenching, masking or inhibitory moiety, thereby generating a signal, wherein detection thereof indicates the presence of the target nucleic acid in the sample as recited in step (d) of claim 47. Furthermore, claim 47 does not require to detect signal increase as argued by applicant.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 40-42, 45, and 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhang *et al.*, (US Patent No. 5,942,391, published on August 24, 1999) in view of Wang *et al.*, (1996).

Zhang *et al.*, teach nucleic acid amplification method: ramification-extension amplification method (RAM).

Regarding claims 40, 41, 45, and 46, since, in a method for detecting a target nucleic acid in a sample, Zhang *et al.*, teach: (a) contacting said nucleic acid in said sample in a reaction vessel under conditions that allow nucleic acid hybridization between complementary sequences in nucleic acids with oligonucleotide probes in the presence of paramagnetic particles coated with a ligand binding moiety, said oligonucleotide probes comprising one or more capture/amplification probes, each having a 3' nucleotide sequence that is neither complementary nor hybridizable to a nucleotide sequence in the target nucleic acid, and a 5' nucleotide sequence that is complementary and hybridizable to a nucleotide sequence in the target nucleic acid, or a 5' nucleotide sequence that is neither complementary nor hybridizable to a nucleotide sequence in the target nucleic acid, and a 3' nucleotide sequence that is complementary and hybridizable to a nucleotide sequence in the target nucleic acid, each capture/amplification probe further having a ligand bound to the non-complementary sequence of the probe, wherein said ligand is capable of binding to and forming an affinity pair with said ligand binding moiety coated onto said paramagnetic particles; said oligonucleotide probes further comprising a circularizable amplification probe having 3' and 5' regions that are complementary to adjacent but noncontiguous sequences in the target nucleic acid, said 3' and 5' regions separated by a linker region that is neither complementary nor hybridizable to a nucleotide sequence in the target

nucleic acid, such that a complex is formed comprising the target nucleic acid, circularizable probe, capture/amplification probes and paramagnetic particles, wherein the capture/amplification probes are hybridized to the complementary nucleotide sequences in the target nucleic acid and are bound to the paramagnetic particles through the binding of the ligand on the capture/amplification probe to the ligand binding moiety on the paramagnetic particles, and the circularizable probe is bound on its 3' and 5' ends to adjacent but noncontiguous sequences in the target nucleic acid; and (c) ligating the 3' and 5' ends of said circularizable probe with a ligating agent that joins nucleotide sequences such that a circular amplification probe is formed (see claim 1 in columns 67-69 and Figure 1), Zhang *et al.*, disclose that the circular oligonucleotide probe is formed by ligating the 3' and 5' ends of a linear oligonucleotide probe (ie., an oligonucleotide probe taught by Zhang *et al.*,) comprising 3' and 5' regions complementary to adjacent sequences in the target nucleic acid under conditions that allow hybridization between complementary sequences in the target nucleic acid and the linear oligonucleotide probe as recited in claim 41. Since, since Zhang *et al.*, teach that, after the circular oligonucleotide probe is formed, the circular oligonucleotide probe contacts with the target nucleic acid, Zhang *et al.*, disclose contacting the nucleic acid with a circular oligonucleotide probe under conditions that allow hybridization between complementary sequences in the target nucleic acid and the circular oligonucleotide probe as recited in (a) of claim 40. Since, in a method for detecting a target nucleic acid in a sample, Zhang *et al.*, further teach: (d) amplifying said circular amplification probe by contacting said complex with a first extension primer that is complementary and hybridizable to a portion of the linker region of the circular amplification probe and a second extension primer that is substantially identical to a

portion of the linker region of the circular amplification probe that does not overlap with the portion of the linker region to which the first extension primer is complementary, dNTPs, and a DNA polymerase having strand displacement activity, under conditions whereby the first extension primer is extended around the circle for multiple revolutions to form a single stranded DNA of repeating units complementary to the sequence of the circular probe, and multiple copies of the second extension primer hybridize to complementary regions of the single stranded DNA and are extended by the DNA polymerase to provide extension products, and whereby the extension products of the second extension primers displace downstream copies of the second extension primers and corresponding extension products of said downstream copies to provide displaced single strands to which multiple copies of said first extension primer bind and are extended by the DNA polymerase; (e) allowing said amplification to proceed until multiple copies of double stranded amplified DNA of varying lengths are produced; and (f) detecting said amplified DNA, wherein detection thereof indicates the presence of the target nucleic acid in the clinical sample, Zhang *et al.,* disclose adding a first primer wherein the first primer comprises (A) a first sequence that is complementary to the circular probe as recited in b) of claim 40, adding a DNA polymerase as recited in c) of claim 40, and detection indicates the presence of the target nucleic acid in the sample as recited in d) of claim 40, the circular probe is amplified using an amplification method selected from the group consisting of polymerase chain reaction, strand displacement amplification, transcription mediated amplification, RAM and primer extension wherein the amplification method is RAM as recited in claims 45 and 46.

Zhang *et al.,* do not disclose adding a primer pair comprising a first primer and a second

primer wherein (i) the first primer of the pair comprises (A) a first sequence that is complementary to the circular probe, (B) a second sequence that is complementary to the second primer of the pair, and (C) a signal generating moiety; (ii) the second primer of the pair comprises (A) a sequence that is complementary to the first primer and (B) a moiety capable of quenching, masking or inhibiting the activity of the signal generating moiety when located adjacent to, or in close proximity to the signal generating moiety; and (iii) when the first primer and the second primer are bound to one another, the signal is inhibited as recited in (b) of claim 40, and detecting a signal which is generated by separating the signal generating moiety and the quenching, masking or inhibitory moiety as recited in (d) of claim 40, and disclose that the signal generating moiety is a fluorescent agent as recited in claim 42.

The teachings of Wang *et al.,* have been summarized previously, *supra.* Wang *et al.,* teach adding a primer pair comprising a first primer and a second primer wherein (i) the first primer of the pair comprises (A) a first sequence that is complementary to the circular probe, (B) a second sequence that is complementary to the second primer of the pair, and (C) a signal generating moiety; (ii) the second primer (ie., the oligonucleotide which is incapable of acting as a primer for said polymerase of the pair taught by Wang *et al.,*) comprises (A) a sequence that is complementary to the first primer and (B) a moiety capable of quenching, masking or inhibiting the activity of the signal generating moiety when located adjacent to, or in close proximity to the signal generating moiety; and (iii) when the first primer and the second primer are bound to one another, the signal is inhibited as recited in (b) of claim 40 and detecting a signal which is generated by separating the signal generating moiety and the quenching, masking or inhibitory moiety as recited in (d) of claim 40 and also teach that the signal generating moiety is a

fluorescent agent as recited in claim 42 (see column 3, second paragraph, columns 19 and 20, claims 1 and 3, and Figure 1).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the method recited in claim 40 wherein (i) the first primer of the pair comprises (A) a first sequence that is complementary to the circular probe, (B) a second sequence that is complementary to the second primer of the pair, and (C) a signal generating moiety; (ii) the second primer comprises (A) a sequence that is complementary to the first primer and (B) a moiety capable of quenching, masking or inhibiting the activity of the signal generating moiety when located adjacent to, or in close proximity to the signal generating moiety; and (iii) when the first primer and the second primer are bound to one another, the signal is inhibited, and wherein a signal which is generated by separating the signal generating moiety and the quenching, masking or inhibitory moiety is detected in view of the patents of Zhang *et al.,* and Wang *et al.*. One having ordinary skill in the art would have been motivated to do so because Wang *et al.,* have successfully detected the target nucleic acid in the sample by detecting a signal which is generated by separating the signal generating moiety and the quenching, masking or inhibitory moiety, and the simple replacement of one well known detection method (i.e., the method taught by Zhang *et al.,*) from another well known detection method (i.e., the method taught by Wang *et al.,*) during the process of detecting the target nucleic acid would have been, in the absence of convincing evidence to the contrary, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made because the detection method taught by Wang *et al..,* would eliminate or reduce nonspecific priming events (see column 7, second paragraph).

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.06.

Response to Arguments

In page 10, third paragraph of applicant's remarks, applicant argues that: (1) "it would not have been obvious to perform the method of claim 40 in view of the method of Wang, since the Wang method, when considered in its entirety, produces a result (i.e., decrease in signal detected upon amplification of the target nucleic acid) that is completely opposite to the method taught in claim 40 (i.e., an increase in the signal upon amplification of the target nucleic acid). Furthermore, the increase in signal in the method of claim 40 actually teaches away from the combined Zhang and Wang methods"; and (2) "[W]ang teaches the use of a blocking oligonucleotide which functions to prevent binding of the double-stranded primer to the target nucleic acid, therefore the primer of the Wang method can only bind to the target nucleic acid as a single-stranded entity. Claim 40 recites that the target nucleic acid and the primer pair are contacted under conditions that allow hybridization between the target nucleic acid and the primer pair. Accordingly, it would not have been obvious to perform the method of claim 40 in the presence of a blocking oligonucleotide, which would only serve to compete with the second primer of the primer pair".

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection. First, claim 40 does not require an increase in the signal upon amplification of the target nucleic acid as argued by applicant. Second, applicant has no evidence

to show that a blocking oligonucleotide (ie., said oligonucleotide) taught by Wang *et al.,* serves to compete with the second primer of Wang *et al.,* (see column 19, claim 1) since Wang *et al.,* do not teach that the blocking oligonucleotide (ie., said oligonucleotide) and the second primer bind to the same region of the target nucleic acid.

7. Claim 43 is rejected under 35 U.S.C. 103(a) as being unpatentable over Zhang *et al.,* (1999) in view of Wang *et al.,* (1996) as applied to claims 40-42, 45, and 46 above, and further in view of Heller (US Patent No. 5,532, 129, published on July 2, 1996).

The teachings of Zhang *et al.,* and Wang *et al.,* have been summarized previously, *supra.*

Zhang *et al.,* and Wang *et al.,* do not disclose that the signal generating moiety (ie., donor) is a chemiluminescent agent as recited in claim 43.

Heller teaches that either a fluorphore or a chemiluminescent group is used as a donor for non-radiative energy transfer (see column 3, second paragraph).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the method recited in claim 43 wherein the signal generating moiety is a chemiluminescent agent in view of the patents of Zhang *et al.,* Wang *et al.,* and Heller. One having ordinary skill in the art would have been motivated to do so because Heller has successfully used a fluorphore or a chemiluminescent group as a donor for non-radiative energy transfer, and the simple replacement of one kind of signal generating moiety (i.e., a fluorescent donor taught by Wang *et al.,*) from another kind of signal generating moiety (i.e., chemiluminescent donor taught Heller) during the process of performing the method recited in claim 43 would have been, in the absence of convincing evidence to the

contrary, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made because either a fluorphore or a chemiluminescent group is used as a donor for energy transfer and they are exchangeable (see Heller, column 3, second paragraph).

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements is such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

Response to Arguments

In page 11, last paragraph bridging to page 12, third paragraph of applicant's remarks, applicant argues that "[A]pplicants maintain that it would not have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the method recited in claim 43, in view of the patents of Zhang and Wang. Furthermore, the deficiencies are not cured by the inclusion of Heller".

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection. First, claim 43 is rejected by combining the prior art from Zhang *et al.*, Wang *et al.*, and Heller and is not rejected by Zhang *et al.*, and Wang *et al.*, as argued by applicant. Second, the prior art from Heller is only used to reject claim 43.

8. Claim 44 is rejected under 35 U.S.C. 103(a) as being unpatentable over Zhang *et al.*, (1999) in view of Wang *et al.*, (1996) and Heller (1996) as applied to claims 40-43, 45, and 46 above, and further in view of Segev (US Patent No. 5, 437, 977, published on August 1, 1995).

The teachings of Zhang *et al.*, Wang *et al.*, and Heller have been summarized previously, *supra.*

Zhang *et al.*, Wang *et al.*, and Heller do not disclose that the signal generating moiety is a an enzyme or enzyme substrate as recited in claim 44.

Segev teaches that non-radiative energy transfer is finished by a suitable chemiluminescent catalyst such as peroxidase and luciferase and a suitable absorber/emitter (see column 7, last paragraph and column 8, first paragraph).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the method recited in claim 44 wherein the signal generating moiety is an enzyme in view of the patents of Zhang *et al.*, Wang *et al.*, Heller and Segev. One having ordinary skill in the art would have been motivated to do so because Segev has successfully used a suitable chemiluminescent catalyst such as peroxidase or luciferase and a suitable absorber/emitter for non-radiative energy transfer, and the simple replacement of one kind of chemiluminescent agent related non-radiative energy transfer method (i.e., the method taught by Heller) from another kind of chemiluminescent agent related non-radiative energy transfer method (i.e., the method taught by Segev) during the process of performing the method recited in claim 44 would have been, in the absence of convincing evidence to the contrary, *prima facie* obvious to one having ordinary skill in the art at the time

the invention was made because the method taught by Heller and the method taught by Segev are functional equivalent methods which are used for the same purpose.

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.06.

Response to Arguments

In page 12, fourth paragraph bridging to page 13, first paragraph of applicant's remarks, applicant argues that "[A]pplicants maintain that it would not have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the method recited in claim 44, in view of the patents of Zhang, Wang, and Heller. Furthermore, the deficiencies are not cured by the inclusion of Segev".

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection. First, claim 44 is rejected by combining the prior art from Zhang *et al.,* Wang *et al.,* Heller and Segev, and is not rejected by Zhang *et al.,* Wang *et al.,* and Heller as argued by applicant. Second, the prior art from Segev is only used to reject claim 44.

9. Claim 49 is rejected under 35 U.S.C. 103(a) as being unpatentable over Wang *et al.,* (1996) as applied to claims 47, 48, 51, and 52 above, and further in view of Heller (1996).

The teachings of Wang *et al.,* have been summarized previously, *supra.*

Wang *et al.,* do not disclose that the signal generating moiety (ie., donor) is a chemiluminescent agent as recited in claim 49.

Heller teaches that either a fluorphore or a chemiluminescent group is used as a donor for non-radiative energy transfer (see column 3, second paragraph).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the method recited in claim 43 wherein the signal generating moiety is a chemiluminescent agent in view of the patents of Wang *et al.*, and Heller. One having ordinary skill in the art would have been motivated to do so because Heller has successfully used a fluorphore or a chemiluminescent group as a donor for non-radiative energy transfer, and the simple replacement of one kind of signal generating moiety (i.e., a fluorescent donor taught by Wang *et al.*,) from another kind of signal generating moiety (i.e., chemiluminescent a taught Heller) during the process of performing the method recited in claim 43 would have been, in the absence of convincing evidence to the contrary, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made because either a fluorphore or a chemiluminescent group is used as a donor for energy transfer and they are exchangeable (see Heller, column 3, second paragraph).

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements is such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

Response to Arguments

In page 13, second to fourth paragraph of applicant's remarks, applicant argues that "[A]pplicants maintain that it would not have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the method recited in claim 49, in view of the patents of Wang. Furthermore, the deficiencies are not cured by the inclusion of Heller".

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection. First, claim 49 is rejected by combining the prior art from Wang *et al.*, and Heller and is not rejected by Wang *et al.*, as argued by applicant. Second, the prior art from Heller is only used to reject claim 49.

10. Claim 50 is rejected under 35 U.S.C. 103(a) as being unpatentable over Wang *et al.*, (1996) and Heller (1996) as applied to claims 47, 48, 51, and 52 above, and further in view of Segev (1995).

The teachings of Wang *et al.*, and Heller have been summarized previously, *supra.*

Wang *et al.*, and Heller do not disclose that the signal generating moiety is a an enzyme or enzyme substrate as recited in claim 50.

Segev teaches that non-radiative energy transfer is finished by a suitable chemiluminescent catalyst such as peroxidase and luciferase and a suitable absorber/emitter (see column 7, last paragraph and column 8, first paragraph).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the method recited in claim 44 wherein the signal generating moiety is an enzyme in view of the patents of Wang *et al.*, Heller and Segev.

One having ordinary skill in the art would have been motivated to do so because Segev has successfully used a suitable chemiluminescent catalyst such as peroxidase or luciferase and a suitable absorber/emitter for non-radiative energy transfer, and the simple replacement of one kind of chemiluminescent agent related non-radiative energy transfer method (i.e., the method taught by Heller) from another kind of chemiluminescent agent related non-radiative energy transfer method (i.e., the method taught by Segev) during the process of performing the method recited in claim 44 would have been, in the absence of convincing evidence to the contrary, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made because the method taught by Heller and the method taught by Segev are functional equivalent methods which are used for the same purpose.

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.06.

Response to Arguments

In page 13, fifth paragraph bridging to page 14, first paragraph of applicant's remarks, applicant argues that "[A]pplicants maintain that it would not have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the method recited in claim 50, in view of the patents of Wang and Heller. Furthermore, the deficiencies are not cured by the inclusion of Segev".

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection. First, claim 50 is rejected by combining the prior art from Wang *et*

al., Heller and Segev, and is not rejected by Wang *et al.,* and Heller as argued by applicant. Second, the prior art from Segev is only used to reject claim 50.

Double Patenting

11. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

12. Claims 40-52 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, 5-9, and 43-52 of copending Application No. 10/719,480. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but examined claims in this instant application are not patentably distinct from the reference claims because the examined claims are either anticipated by, or would have been obvious over, the reference claims. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225

USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969). Although independent claims 40 and 47 in this instant application are not identical to claims 1 and 43- 46 of copending Application No. 10/719,480, claims 1 and 43-46 of copending Application No. 10/719,480 are directed to the same subject matter and fall entirely within the scope of claims 40 and 47 in this instant application. In other words, claims 40 and 47 in this instant application are anticipated by claims 1 and 43-46 of copending Application No. 10/719,480. Note that claims 42-46 and 48-52 are identical to claims 2, 5-9, and 47-52.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

In page 14, second paragraph of applicant's remarks, applicant argues that "[A]pplicants will consider filing a terminal disclaimer in compliance with 37 C.F.R. 1 .321(c) showing that the conflicting copending application and instant application are commonly owned, upon the Examiner's indication of allowable claims".

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection because applicant has not submitted a terminal disclaimer.

Conclusion

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. No claim is allowed.

15. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is (571)273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (571)272-0745.

Any inquiry of a general nature or relating to the status of this application should be directed to the Chemical Matrix receptionist whose telephone number is (703) 308-0196.

Frank Lu
PSA
February, 2005

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER

3/1/05